Naval Health Research Center Surveillance for Meningococcal Disease

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ABSTRACT Historically, meningococcal disease has had a devastating impact on U.S. military personnel, but since the introduction of a vaccine in the 1970s, rates have dropped over 90%.[1] Department of Defense instructions mandate a meningococcal vaccine for all service personnel. In the last 5 years, rates of meningococcal disease in the military are similar to the U.S. general population. The active duty incidence was 0.21 cases per 100,000 person-years from 2013–2017. Six cases occurred in the 6 months between September 2016 and February 2017; of these, only one was determined to be a vaccine-covered strain. Ongoing surveillance shows vaccination has resulted in a dramatic reduction in meningococcal cases in the military; however, it also demonstrates cases continue to occur sporadically. The recent emergence of new cases reminds us that surveillance and accompanying research are important for evaluating changes in the disease and informing new vaccine development and policy.

INTRODUCTION

Meningococcal disease has historically been associated with military populations, particularly during periods of mobilization. The pathogen, Neisseria meningitidis, can cause a severely debilitating and potentially life-threatening infection. It can present as meningitis or septicemia, and strikes quickly, requiring emergency response when signs and symptoms are noticed. Its case fatality rate is approximately 10% even with antibiotic treatment, and the percentage of cases with seriously debilitating sequelae is approximately 15%.[1] Rates of meningococcal disease were once far higher in the U.S. military than in the U.S. general population, with incidence in U.S. Army personnel over 100 per 100,000 person-years during the first and second world wars.[2,3] Over the last 5 years, military rates have approximated those of the age-adjusted general population, which itself has seen a substantial decline over time.[4] This can be attributed to the effect of meningococcal vaccines.[5] Meningococcal vaccination was first introduced to the military in the early 1970s, and with subsequent vaccine improvements, rates had fallen over 90% by the late 1990s.[6] During 2007–2008, the quadrivalent conjugate vaccine (MCV-4) replaced the quadrivalent polysaccharide (MPSV-4) which had been used since the 1980s, both of which cover serogroups A, C, W, and Y, and rates have continued to fall.

It was previously reported that the incidence in military personnel receiving MCV-4 was 0.298 cases per 100,000 person-years from 2006 through 2013, compared to 0.410 cases per 100,000 person-years in MPSV-4 recipients from 2000 through 2013.[7] In this article, we report incidence data through 2017.

MATERIALS AND METHODS

Passive and active surveillances are conducted through collaboration with state and local public health laboratories, the Armed Forces Health Surveillance Branch, the Navy and Marine Corps Public Health Center, and by contacting sites with cases. Isolates, blood or cerebrospinal fluid samples are collected and shipped to the Naval Health Research Center (NHRC) for conventional bacteriology including serogrouping, and for molecular analysis as described previously.[3] Individual laboratory results are reported to sites, and surveillance data are made available to the public and scientific community through monthly reports.[7] The study population was all active-duty service members, including Air Force, Army, Coast Guard, Marine Corps, and Navy.

The NHRC IRB determined that the surveillance constitutes public health surveillance and not human subjects research.

RESULTS

Between 2006 and the end of 2017, the NHRC Meningococcal Surveillance recorded 44 confirmed or probable meningococcal cases in U.S. active duty service members. Six of these were

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fatal, the last occurring in 2011. In nine cases, no serogroup is available, either because no laboratory results are available or no assay was able to identify a serogroup. Of the serogrouped cases, 40% were serogroup B, 23% C, and 37% Y. However, no serogroup C case has been seen since 2013, and of the six serogrouped cases since 2014, five were B. Epidemiology on cases from 2006 to 2013 has been previously reported.[3,8]

There have been notable periods with no identified cases, specifically a period of over a year during 2011–2012, and of just over 2 years from the middle of 2014 to the middle of 2016. Conversely, seven cases occurred in the 9 months between September 2016 and May 2017, but only two of these were related to each other.

The three cases from 2013 had been vaccinated with MPSV-4, two of which were vaccine failures: a serogroup Y case 12 years from vaccination and a serogroup C case 5 years from vaccination. All of the 11 cases during 2014–2017 had been vaccinated with MCV-4, but only one, a serogroup Y case, could be definitely attributed to vaccine failure. In 5 of the others no serogroup could be identified and 5 were serogroup B.

Overall incidence declined from 0.271 cases per 100,000 person years during the period of 2006–2013, to 0.206 cases during 2013–2017.[7] It was previously reported that from 2000 to 2013 incidence of *vaccine-covered serogroup* cases in personnel with a history of only MPSV-4 vaccination was 0.307 cases per 100,000 person-years, compared to personnel vaccinated with only MCV-4 from 2006 to 2013 of 0.183.[7] More recently, we found vaccine-covered serogroup incidence for MPSV-4 from 2000-2017 to be 0.283, and for MCV-4 from 2006 to 2017 to be 0.106. However, it must be cautioned that the four cases vaccinated with MCV-4 from 2016 and 2017 that were not serogroupable are not included in the numerator. However for three of these, polymerase chain reaction was not able to identify a genogroup, so they are likely to be truly neither A, B, C, Y, or W. For the fourth, no grouping assay was run at the site of the case and no further sample was available.

Figure 1 shows a comparison from 2000 to 2017 of all cases and vaccine-covered cases, with the caveat that the vaccine-covered cases do not include cases of unknown serogroup that might be vaccine-related. Again, in three cases they were likely not vaccine-related, in the other two it is still possible. (One from 2014 was identified alternately as several serogroups in different testing).

From 2013 to 2017, 4 of the 14 cases were aged 17–19, 5 were 20–24, 3 were 25–29, and 2 were at least 30 years old. Of these 14, 6 were Marines, 3 Army, 2 Navy, and 3 Air Force. Two of the 14 cases were female. In addition, three were recruits (all Marines) and one was a service academy student.

Table I shows the surveillance data from 2006 to present. It can be seen that among services, the Marine Corps bears the highest rate of disease, and recruits have much higher rates that than the rest of the military population. Significantly, most of the recruits with disease are Marines

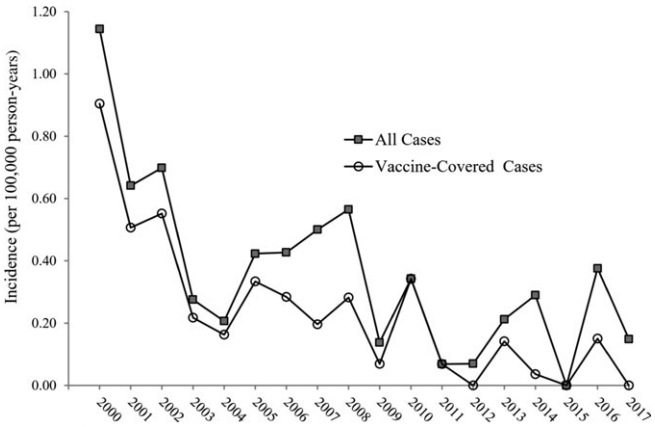

FIGURE 1. Meningococcal cases in active-duty U.S. military since 2000, by cases known to be vaccine failures and all cases. The transition from quadrivalent polysaccharide vaccine (MPSV4) to quadrivalent conjugate vaccine (MCV-4) occurred during 2007–2009. Unknown serogroups were found as follows: 2006: 1; 2007: 1; 2008: 1, 2014: 1; 2016: 2; 2017: 2. However, in both of the 2016 cases and 1 of the 2017 cases the lack of polymerase chain reaction identification of A, B, C, Y, or W suggests that the organism was none of these, and thus truly not vaccine covered.

(12 of the 15 cases from 2006 to 2017). As the recruit population is smaller among the Marine Corps than Navy, Air Force, or Army, the service-specific incidence is extremely high (11.55 cases per 100,000 person-years). Incidence is also significantly higher in the 17–19 years old age group than in the other age groups.

DISCUSSION

Meningococcal disease incidence in the U.S. military is at a historic low, including a 2-year period during 2014–2016 where no cases were reported. The overall incidence of 0.206 cases per 100,000 person-years over the last 5 years, from 2013 to 2017, compares favorably with that of the age-adjusted general U.S. population, in which the incidence ranged in 2016 from 0.09 in 24–44 year olds to 0.21 in 16–23 year olds.[9] We attribute the current rates largely to the success of the vaccines. Moreover, recent data suggest that rates are lower during the nearly 10 years' experience with MCV-4 compared with the prior vaccine, MPSV-4, which had been in use since 1982. This is true among both vaccine-covered and non-vaccine-covered cases. However, concomitant with the increased use of MCV-4 in the military population, has been the introduction of the meningococcal conjugate vaccine to the pediatric vaccine schedule in the civilian population. As more children are vaccinated, it is possible that the historically low rates currently seen in the military are the result of the military vaccination being the second or even third dose of the vaccine.

The effect of the vaccines on the incidence of particular serogroups is difficult to explain, though geographical distribution of serogroups likely plays some role. For example, serogroup A is relatively rare in the USA, but common in Africa. In the USA, the three most common are B, C, and Y.

TABLE I. Meningococcal Disease in the U.S. Military, 2006–2017

Variable	'06	'07	'08	'09	'10	'11	'12	'13	'14	'15	'16	'17	Total '06–'17	Total '13–'17	Incidence '13–'17
Serogroup															
B		3	3	1			1	1	3		2		14	6	
C	4	1			2			1					8	1	
W													0	0	
Y		2	4	1	3	1		1			1		13	2	
Not Determined	2	1	1						1		2	2	9	5	
Mortality status															
Fatal	1	2	2			1							6	0	0% of all
Not fatal	5	5	6	2	5		1	3	4		5	2	38	14	100% of all
Immunizations[a]															
MPSV-4	6	2	4		1			3					16	3	
MCV-4		2	4	2	4	1	1		4		5	2	25	11	
Unknown		3											3	0	
Service															
Air Force			1		1			1	1		1		5	3	0.19
Army	2	4		1	1				1		1	1	11	3	0.12
Coast Guard		1											1	0	0.00
Marines	4		6		3	1		2	2		2		20	6	0.64
Navy		2	1	1			1				1	1	7	2	0.12
AD status															
Recruit[b]	3	1	5		2	1			1		3		16	4	2.29
Enlisted	3	6	3	2	3		1	2	3		2	2	27	9	0.20
Officer								1					1	1	0.12
Gender															
F			1	1	2	1			1		1		7	2	0.19
M	6	7	7	1	3		1	3	3		4	2	37	12	0.19
Race/Ethnicity															
Asian			1						1				2	1	0.34
Black	1	3	1		3	1			2		1	1	13	4	0.35
Hispanic			1				1	1			1		4	2	0.26
White	5	3	5	1	2			2	1		2	1	22	6	0.13
Unk/Other		1		1							1		3	1	0.74
Age															
17–19	3	3	5		1	1			2		2		17	4	0.91
20–24	3		2	2	3		1		1		2	2	16	5	0.24
25–29		2			1				1		1		5	2	0.13
30–34								2					2	2	0.19
≥35		2	1					1					4	1	0.07
Total cases	6	7	8	2	5	1	1	3	4	0	5	2	46	14	
Incidence	0.43	0.50	0.57	0.14	0.34	0.07	0.07	0.21	0.29	0.00	0.38	0.15[c]	0.26[c]	0.21[c]	

(AD = Active Duty; MCV-4 = quadrivalent conjugate vaccine; MPSV-4 = quadrivalent polysaccharide vaccine).

Data Sources: Navy and Marine Corps Public Health Center, EpiData Center, Armed Forces Health Surveillance Branch, and Naval Health Research Center.

[a]The counts here do not imply vaccine failures.

[b]Includes two service academy students.

[c]Estimated 2017 total population size denominator.

Yet in the military, since 2007, around the time of the introduction of MCV-4, only 4 serogroup C cases have been recorded, with none after 2013. Most of the subsequent cases have been serogroups B and Y. Interestingly, the vaccines used in the military have never covered serogroup B, yet it does not appear serogroup B exploited reduced "competition" from the vaccine-covered serogroups – the incidence of serogroup B cases did not rise. That said, in the last 3 years, of the six serogrouped military cases five were B and one Y (serogroup not attainable for the other five cases). With meningococcal disease being relatively rare in the military, it is difficult to draw conclusions from a few cases over 3 years, especially since we do not have definitive serogroup data on two of the cases. Looking forward, it is possible that mainly serogroup B cases will be seen in the military, but it may simply be that the recent disproportionate number of B cases is a temporary anomaly. In 2013, for example, it was thought possible that serogroup Y was becoming predominant, based on a few years of recent data, but that predominance never materialized. A natural question is whether recent experience is sufficient reason to make a serogroup B vaccine mandatory for military recruits. After several cases in late 2016 and early 2017, there were no cases in the last 7 months of 2017.

CONCLUSION

The development of a meningococcal vaccine in the late 1960s and early 1970s by Goldshneider, Artenstein, and Gotschlich[10,11] must be considered one of the greatest successes of military medicine, as a disease whose incidence in the military was once far in excess of the general population now occurs at about the same rate as the general population. Moreover, treatment of the disease has also made impressive gains, as the military has experienced no fatalities since 2011. In order to understand current rates and to see continued decreases in incidence, it may be advisable to examine the number of MCV-4 doses recruits have already received before they enter the military, and to consider this in the context of the effect a serogroup B vaccine might have on recruits. Continued surveillance will be a key to this effort.

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PRESENTATIONS

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14. ABSTRACT

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